Pharmacological Interventions for Substance Abuse

Missouri Spring Training Institute
May 29, 2003

Nick Reuter
Division of Pharmacological Treatment
Center for Substance Abuse Treatment
Substance Abuse and Mental Health Services Administration

Overview

- Introduction - CSAT
- National Trends in Opiate Abuse
- CSAT Mission/Programs
- Opioid Tx Innovations
  - Opioid Treatment Program Regulation – the first year
  - Office-Based Treatment
    - legislation
    - medications
- Next Steps, Challenges

Objectives

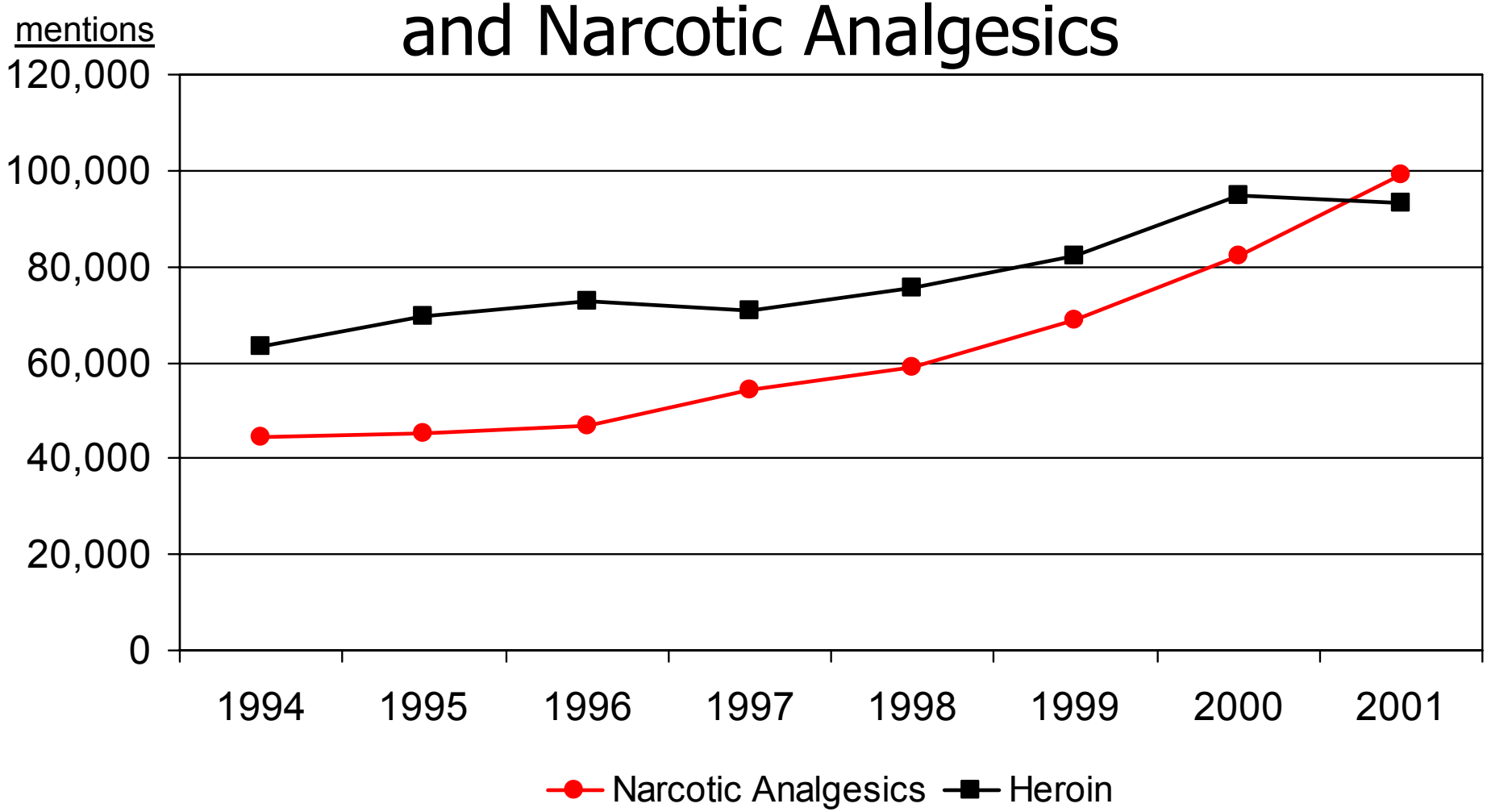
- Overview of Opioid Program **and** Office-Based Treatment Oversight System
- Understand Federal Physician Certification System
- Emerging Implementation Issues
- Methadone Associated Mortality

Scope of the Public Health Problem

- An estimated 2.4 million people have used heroin at some time in their lives

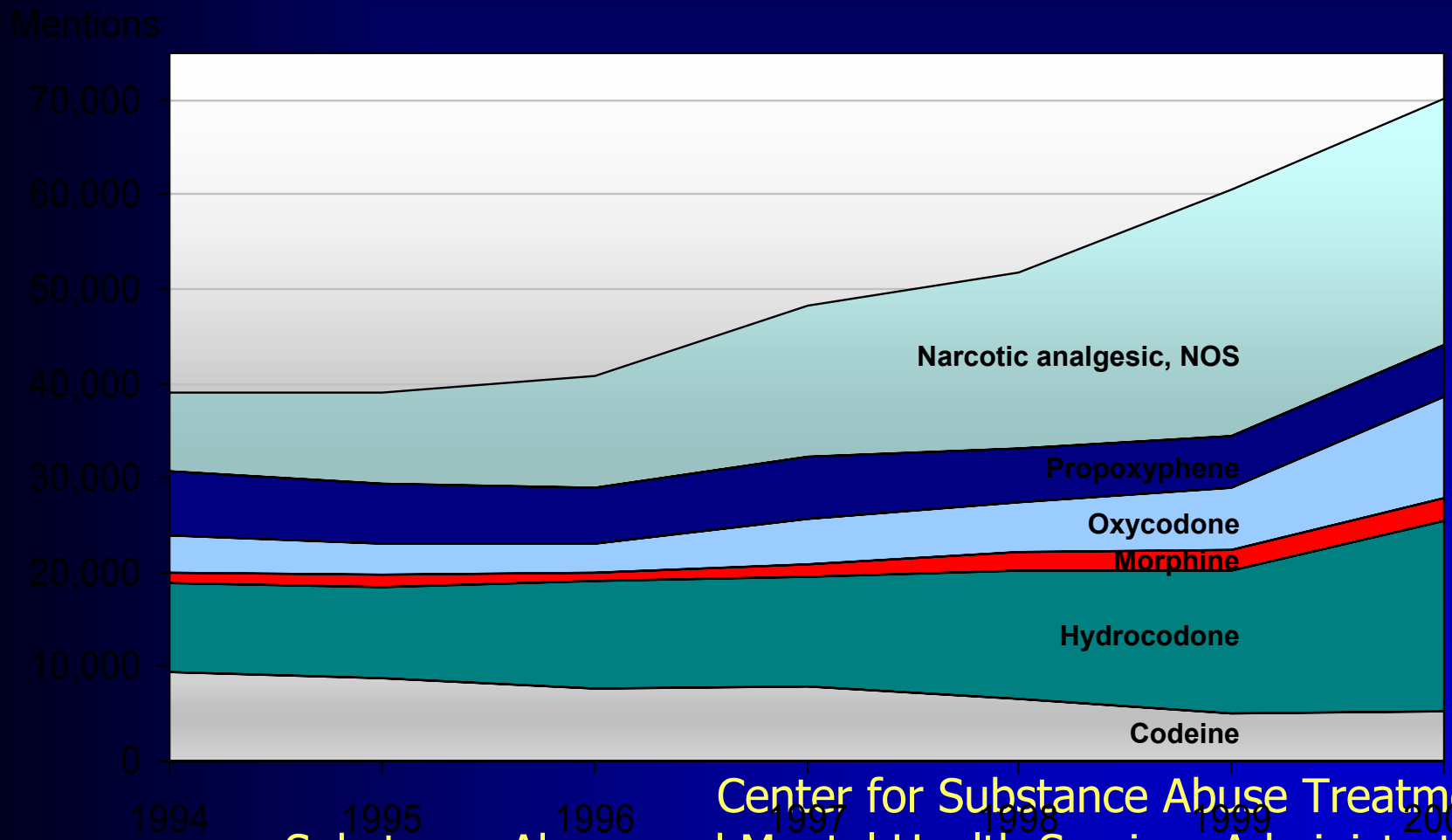
  (NHSDA, 1998)
- During 1996 through 1998, an estimated 471,000 persons used heroin for the first time. Of them, 25% were under age 18 and another 47% were age 18 - 25 (NHSDA, 1999)

DAWN
ED Mentions of Heroin and Narcotic Analgesics



Source: Drug Abuse Warning Network

ED Mentions of Narcotic Analgesics



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Source: Drug Abuse Warning Network

Narcotic Analgesics, 2000

	ED Mentions	% change from 1998	% change from 1999
NOS	25,935	+40%	n.s.
Hydrocodone	20,098	+48%	+32%
Oxycodone	10,825	+108%	+68%
Propoxyphene	5,485	n.s.	n.s.
Codeine	5,295	-20%	n.s.
Morphine	2,483	n.s.	n.s.

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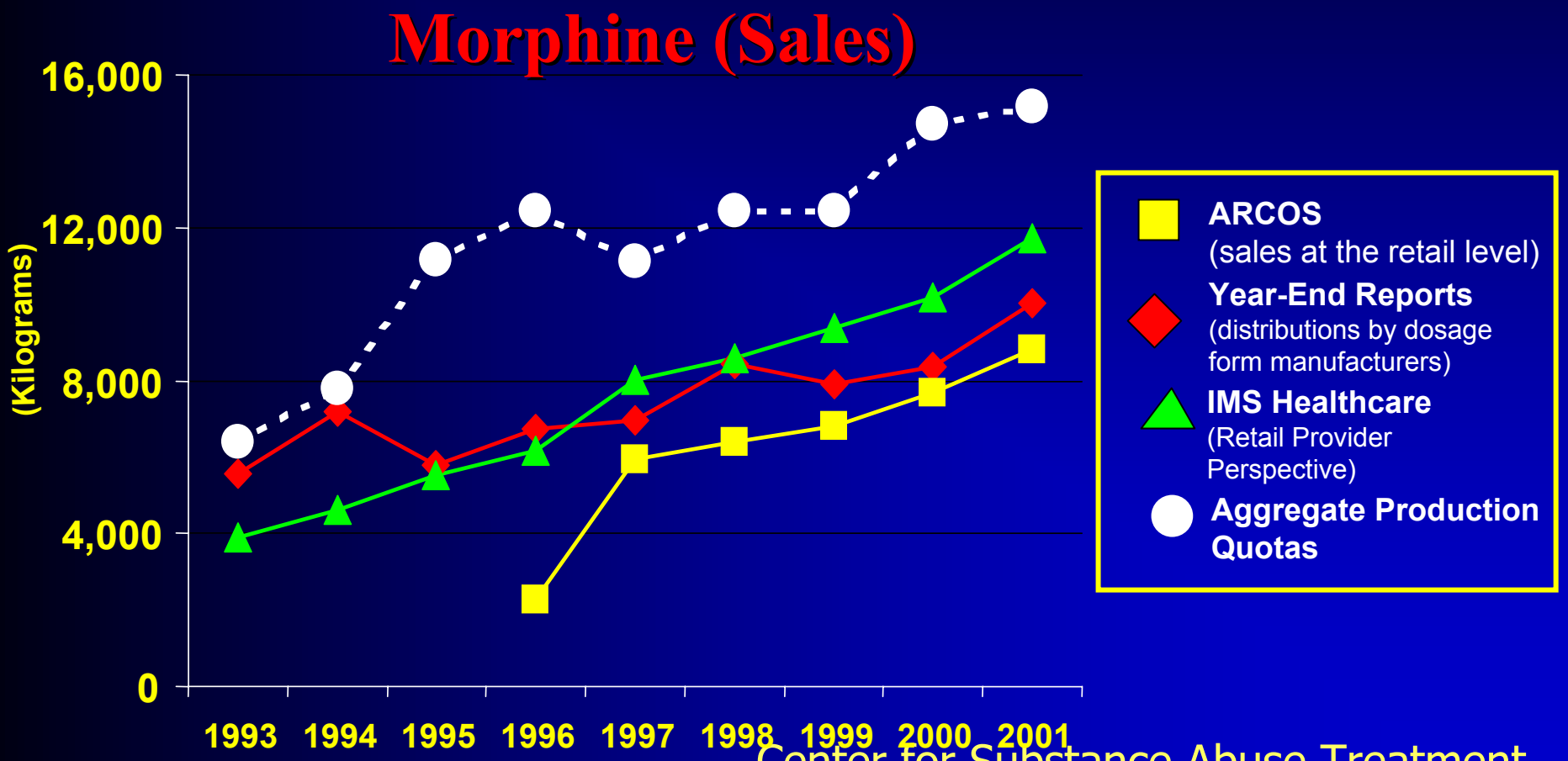
Source: Drug Abuse Warning Network

SAMHSA's Drug Abuse Warning Network (DAWN)

- Narcotic prescription pain reliever related visits to emergency rooms increased from 1994-2001
  - 352% increase in oxycodone mentions
  - 230% increase in methadone mentions
  - 210% increase in morphine mentions
  - 131% increase in hydrocodone mentions

Estimates of U.S. Consumption



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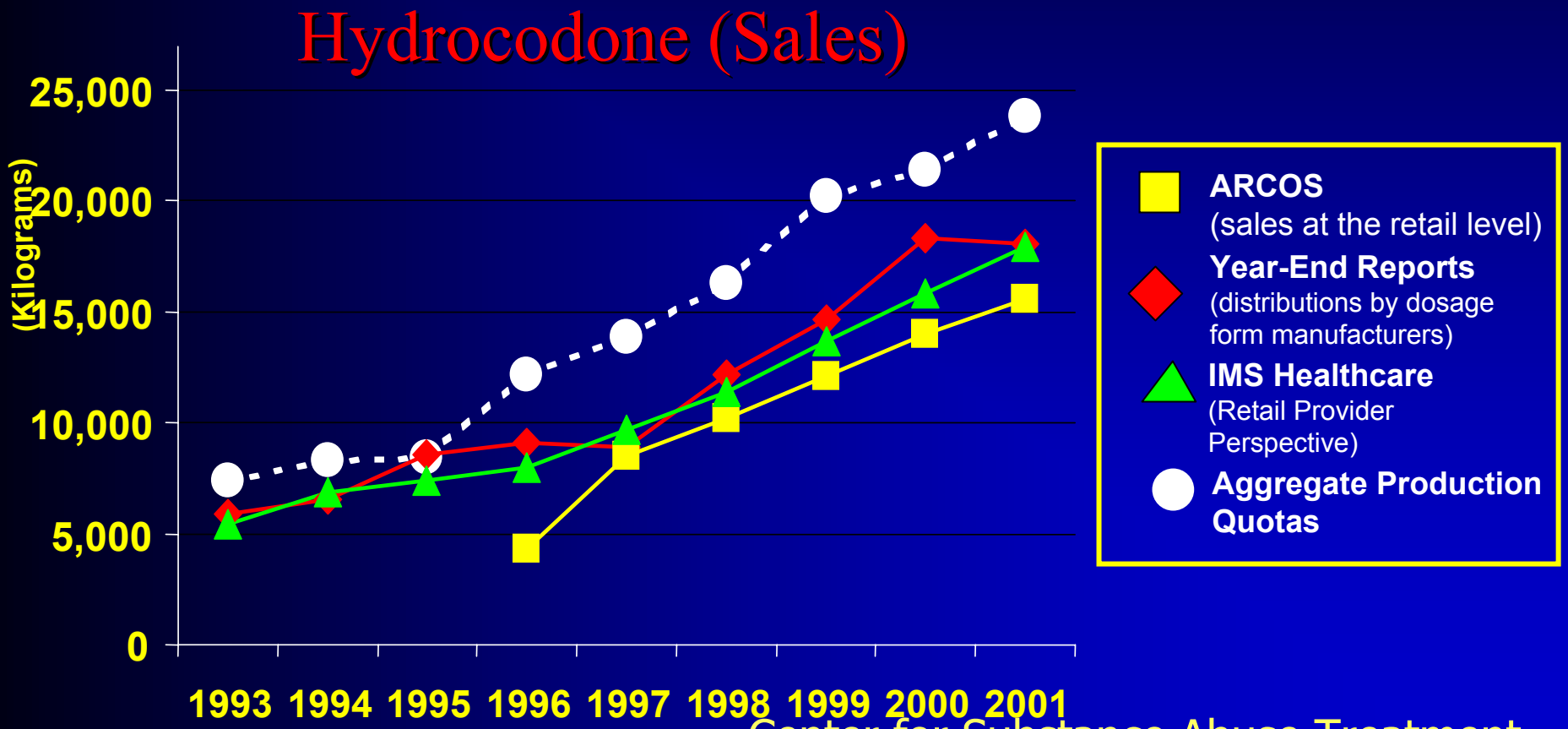
Estimates of U.S. Consumption



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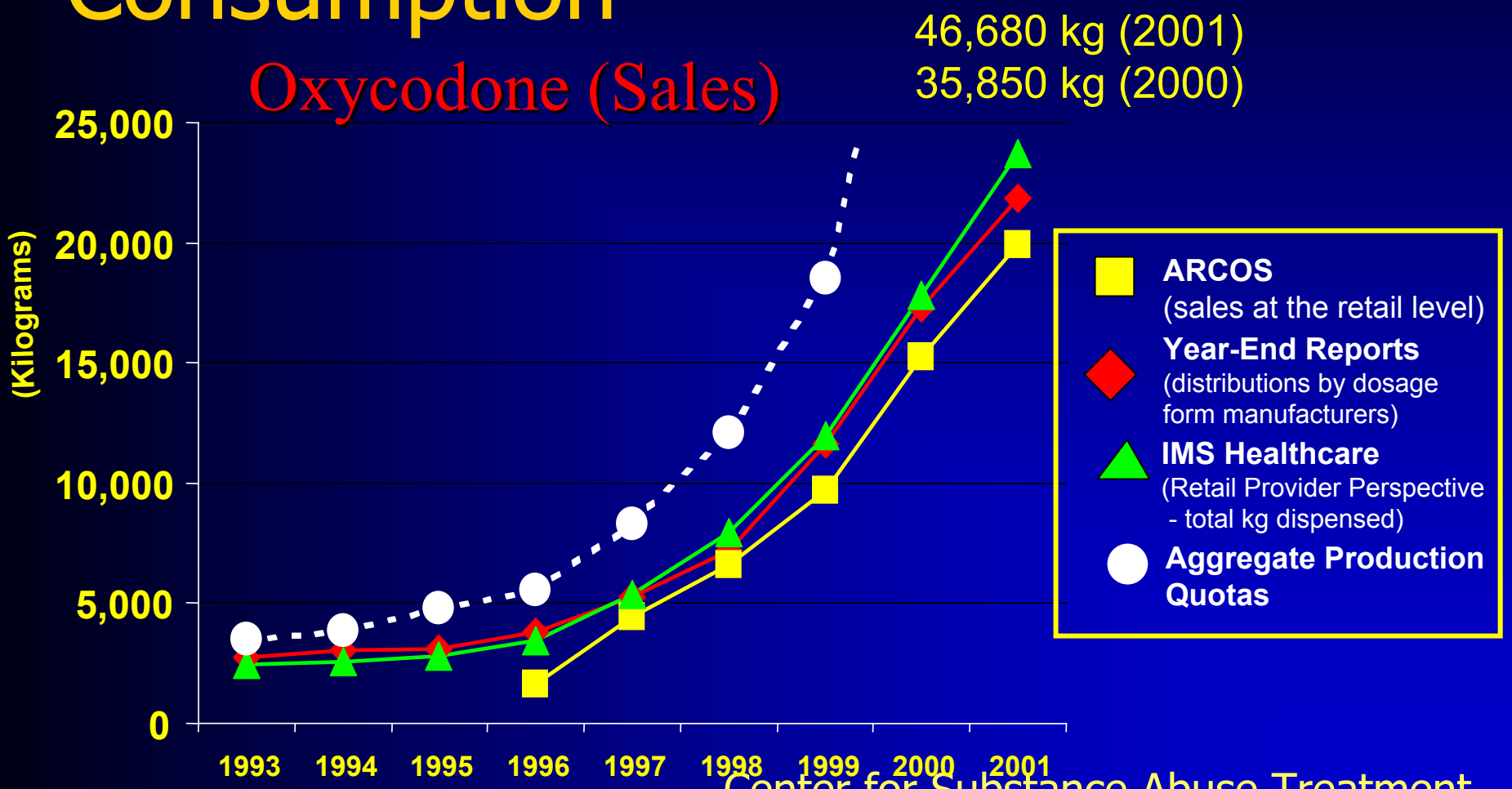
Estimates of U.S. Consumption



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What about abuse?

- According to the National Institute on Drug Abuse (NIDA), in 1999 Four million Americans reported current use of prescription drugs for non-medical purposes
- The most dramatic increases were found among the 12 to 25 year olds
- Oxycontin® and Ritalin® were among the most cited abused medications

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Current Situation *cont.*

SAMHSA's Drug Abuse Warning Network (DAWN)

- Between 1998 and 2000 there were more new users among the 12 – 17 year olds than among the 18-25 year olds
- Past year use was 12% in 2001, up from 9% in 2000 for young adults

SAMSHA/CSAT Mission

The Center for Substance Abuse Treatment(CSAT) of the Substance Abuse and MentalHealth Services Administration (SAMHSA),U.S. Department of Health and Human Services (DHHS), was created in October 1992 with a congressional mandate to expand the availability of effective treatment and recovery services for alcohol and drug problems.

SAMHSA/CSAT Programs

- Substance Abuse Prevention Treatment Block Grant
  - $1.7 billion, nationwide
  - Technical Assistance
- Other Grants
- Treatment Guidelines
- Opioid Treatment Oversight

Type of Substance Abuse Tx

- Drug Free Residential, TC
- Inpatient
- 12-step, NA, AA,
- Faith based
- Out-patient drug free
- Opioid Assisted Treatment
  - Detoxification
  - Maintenance

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DATA (Drug Addiction Treatment Act)

The Children's Health Act of 2000

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DATA (Drug Addiction Treatment Act)

- Permits the prescribing of a schedule III, IV or V opioid treatment drug, approved by FDA for maintenance or detoxification treatment

DATA (Drug Addiction Treatment Act)

- Limits Patients
  - The total number of patients for a practitioner or group practice will not exceed 30
  - Secretary may, by regulation change this number

DATA (Drug Addiction Treatment Act)

- Limits medications
  - Schedule III, IV, or V (narcotics)
  - Approved by the FDA for use in maintenance or detoxification treatment
  - Have not been the subject of an adverse determination

DATA (Drug Addiction Treatment Act)

- Limits eligible physicians
  - Physician holds a subspecialty board addiction certification
    - ASAM
    - American Board of Medical Specialties
    - American Osteopathic Association

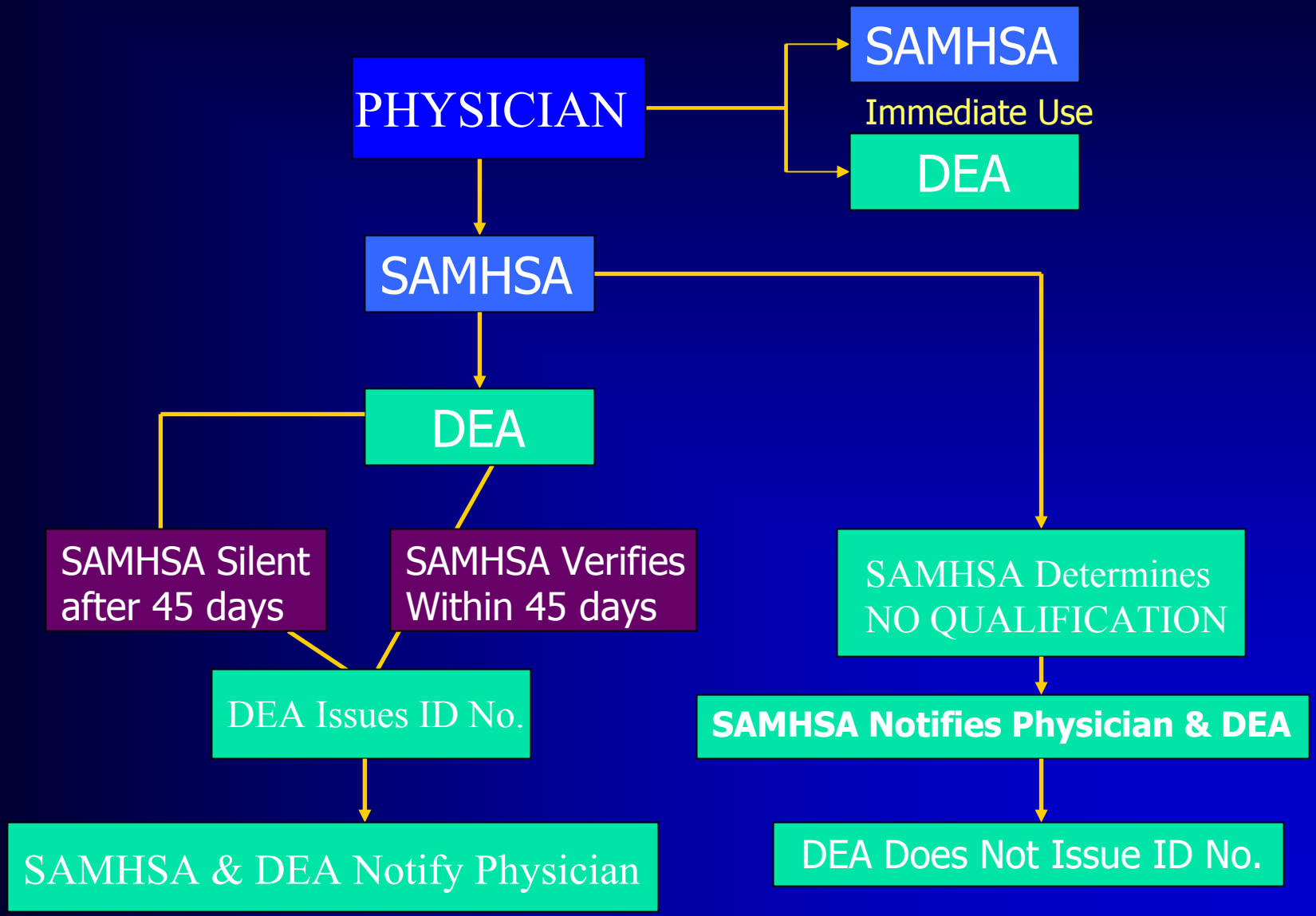
Premption of State Laws

- For three years, a State may not preclude a practitioner from dispensing or prescribing narcotic drugs to patients for maintenance or detoxification, unless the State enacts a special law prohibiting the practitioner from prescribing or dispensing. (extended to 10/08/05)

State Actions

- NY State emergency regulations
- Register physicians (must renew)
  - Linkage agreement with authorized substance abuse treatment services provider
  - CME – 8 hours every two years
- Report patients they dispense to
- Register Pharmacies

OFFICE-BASED TREATMENT NOTIFICATION REVIEW



Notification Submission

Form to facilitate notifications

- SMA-167

- Notifications may be submitted:
  - By mail
  - By fax
  - Online

Address to Submit Notification of Intent

Substance Abuse and Mental Health Services Administration

Center for Substance Abuse Treatment

Division of Pharmacologic Therapies

Attn: Opioid Treatment Waiver Program

5600 Fishers Lane, Rm. 12-105

Rockville, MD 2085

Fax: (301) 443-3994

SMA - 107 Information Collected

- Name, address, telephone, fax, email,
- Medical license, DEA registration
- Group practice status
- Credentialing and/or training
- Certifications
  - Patient max
  - Medications used
  - Capacity to refer

Notification Verification

- Signed
- Confirm Certifications
  - 30 patients
  - FDA Approved, CSA III Medications
  - Capacity to refer
- Confirm active license to practice medicine
  - Some cases direct contact w/Medical Boards
- Confirm credentialing, or
- Confirm 8-hour training
- Verify from DEA, registration status
  - Authorized to prescribe schedule III narcotics

Buprenorphine Waiver Status

- 1600 Notifications Submitted
- Most physicians indicate training
- Most physicians agree to listing on S-Treatment Facility Locator
- 1400 Waivers Approved.

ASAM Buprenorphine Trainings - Demographics

Years since graduating medical school 23.5 (1-68)

Specialty

183 (31%) Psychiatry

150 (28%) Addiction Medicine

133 (23%) Internal Medicine

106 (18%) Family Practice

15 (3%) Addiction Psychiatry

Certification

214 (36%) ASAM

25 (4%) ABPN

30 (5%) ASAM/ABPN

4 (< 1%) ASAM/AOAAM

ASAM Buprenorphine Trainings – Clinical Experience

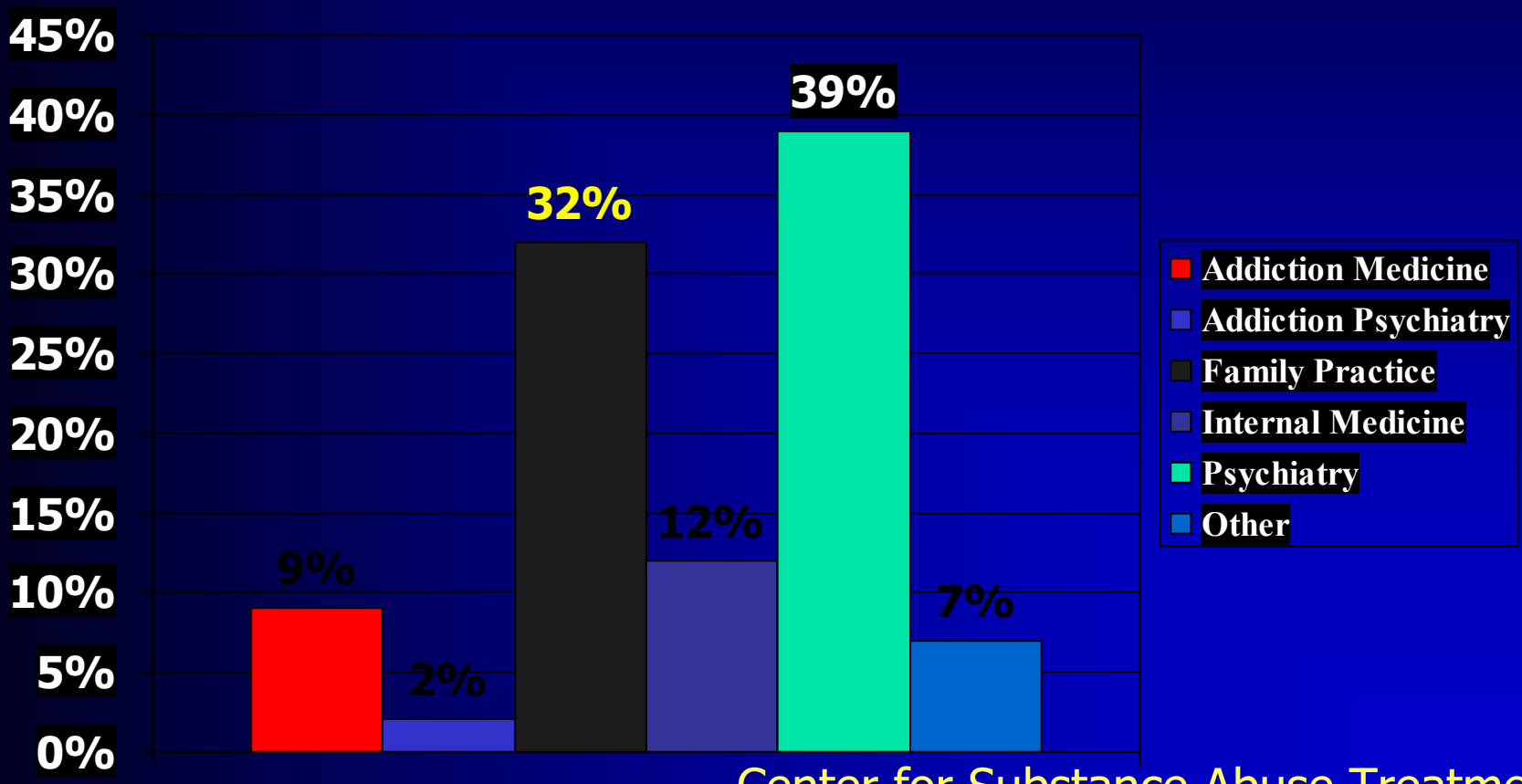
Experience treating opioid dependent patients

- 28 (5%) No experience
- 55 (10%) Detoxification only
- 235 (41%) Methadone maintenance
- 36 (6%) Medical or psychiatric comorbid conditions, not addiction
- 80 (14%) Abstinence based treatment
- 100 (24%) Other

Length of time treating opioid dependent patients

- 34 (7%) Less than one year
- 72 (13%) One to three years
- 436 (80%) Greater than three years

Reported Primary Specialties of Physician Trainees (N= 394)



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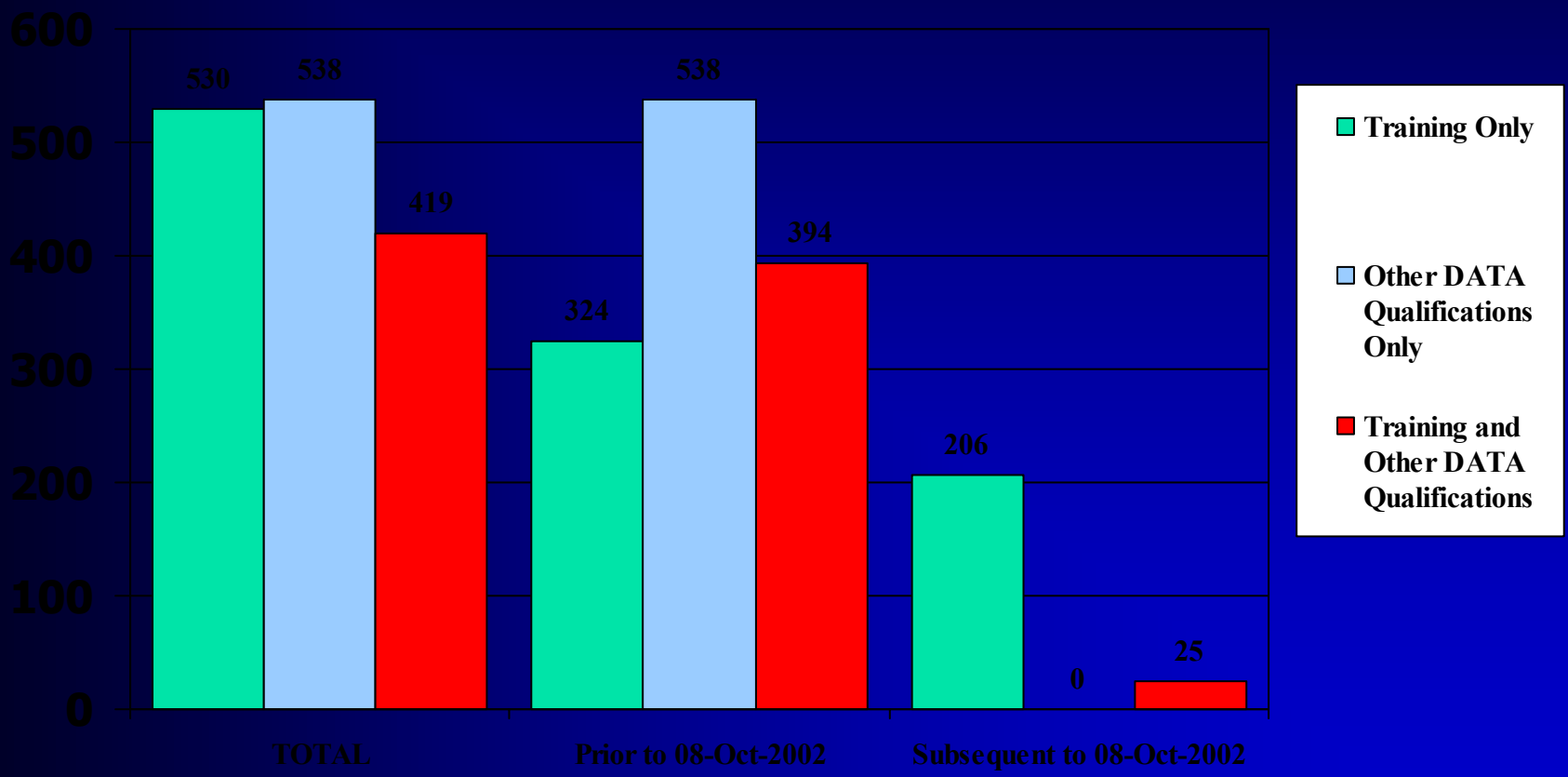
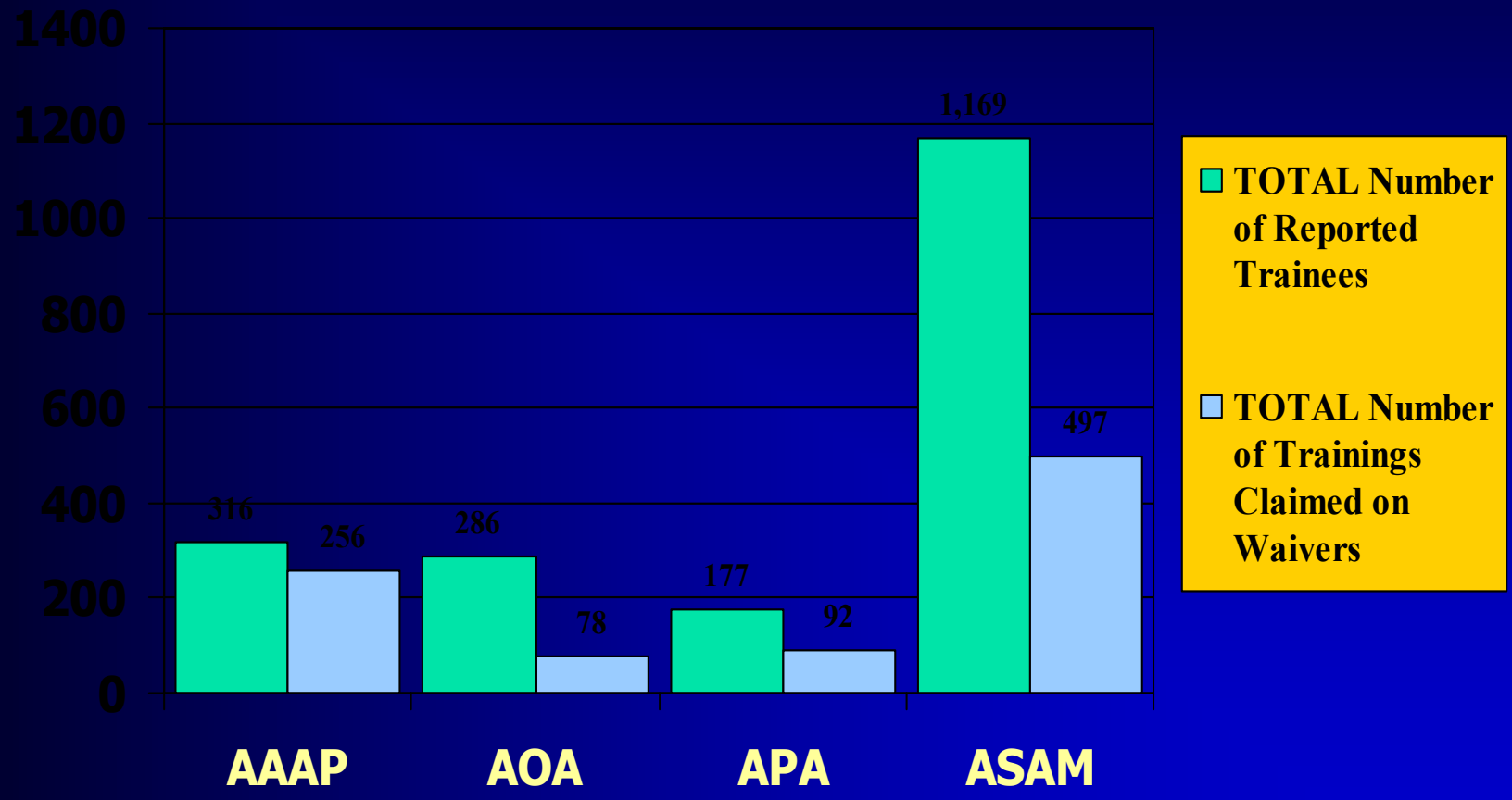
Submitting Waiver Notifications by Time Period



Trainees Reported vs Trainings Claimed by Training Group



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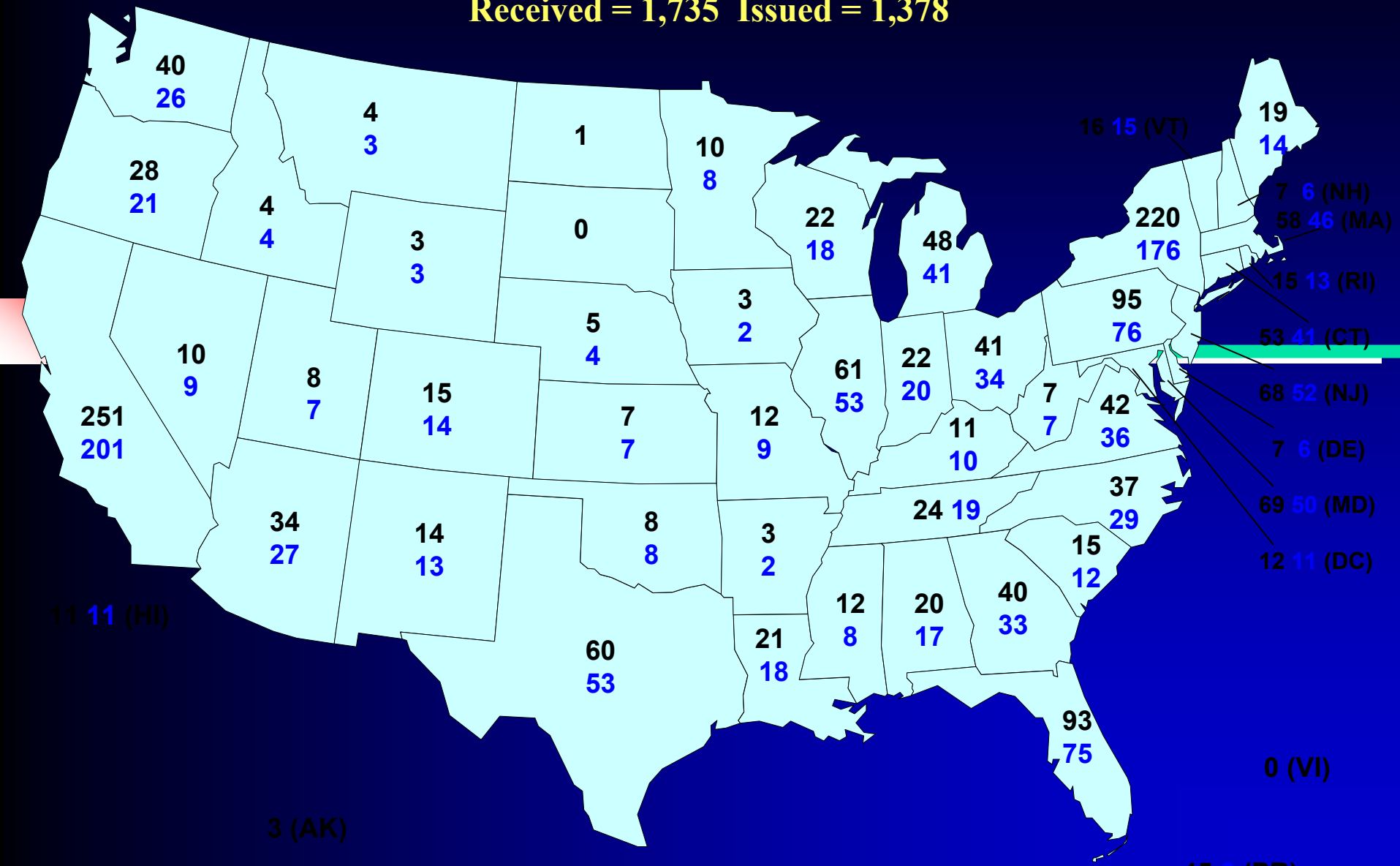
Online Trainings

- 82 reported online trainees
- Reported Trainings
  - 4.3% of total trainees
  - 81 persons (1 completed 2 online trainings)
  - Available only through APA and AAAP currently

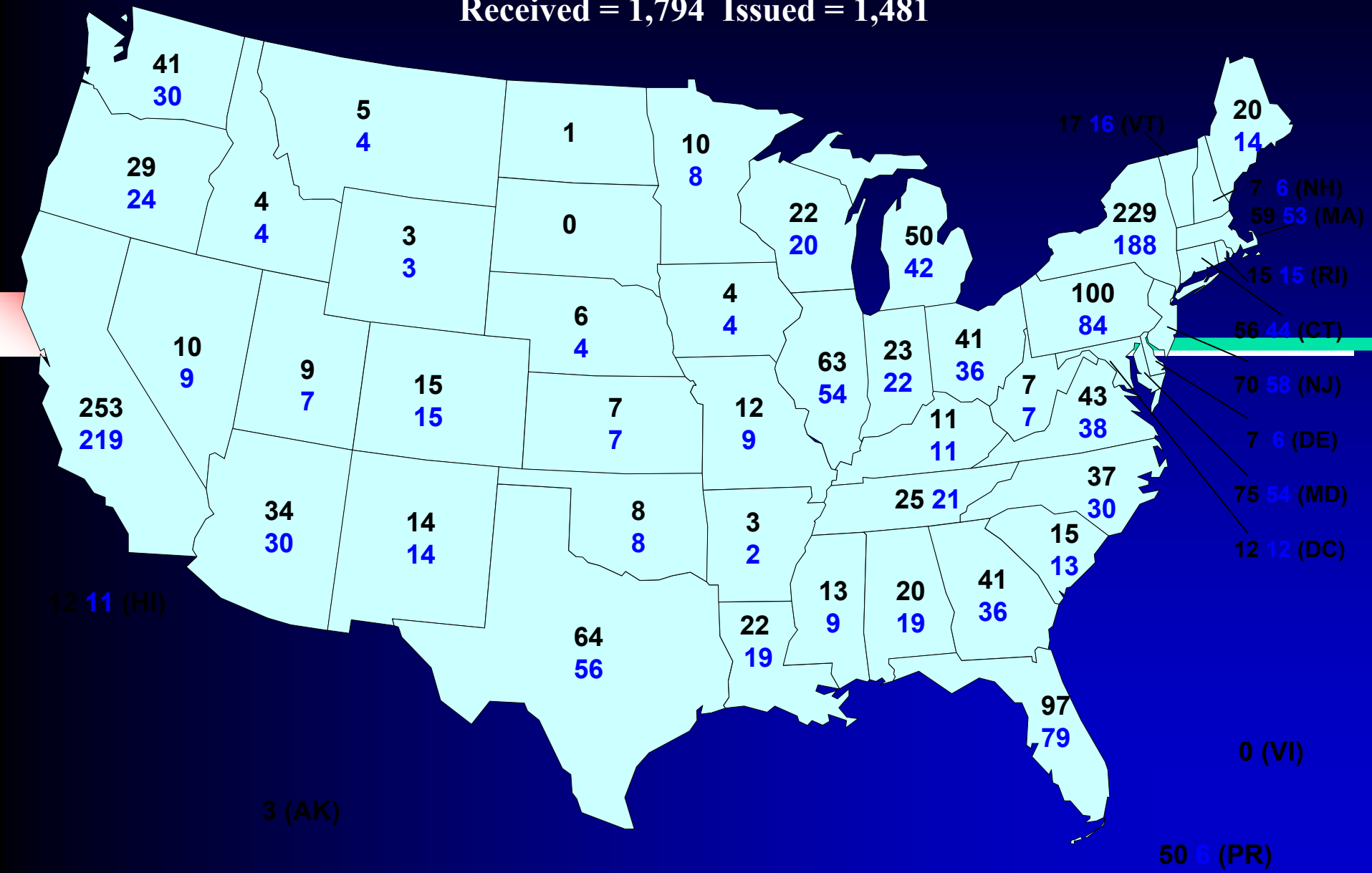
Waiver Notifications by State as of May 2, 2003

Received = 1,735 Issued = 1,378

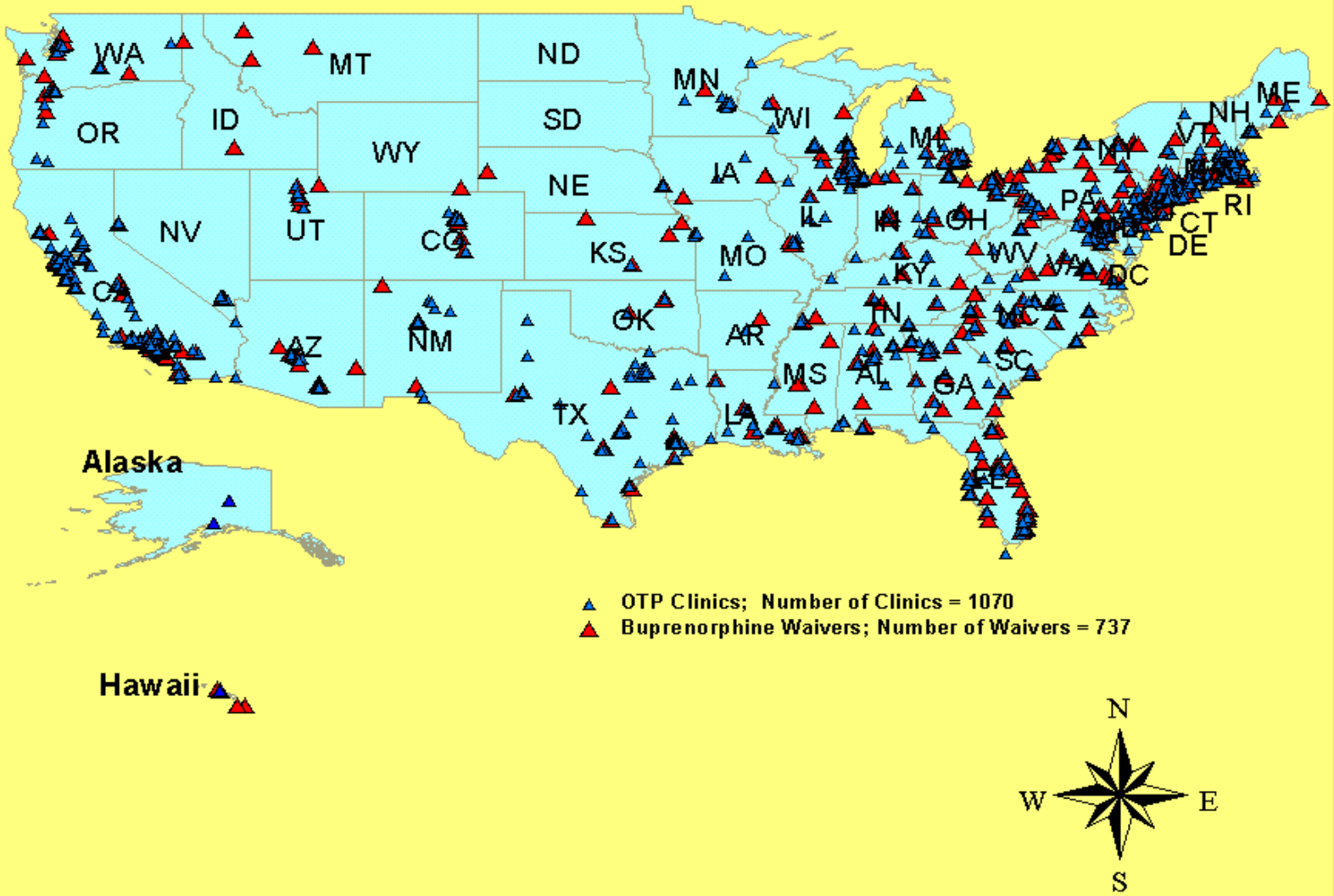


Waiver Notifications by State as of May 23, 2003

Received = 1,794 Issued = 1,481



OTP Clinics and Buprenorphine Waivers



Subutex®

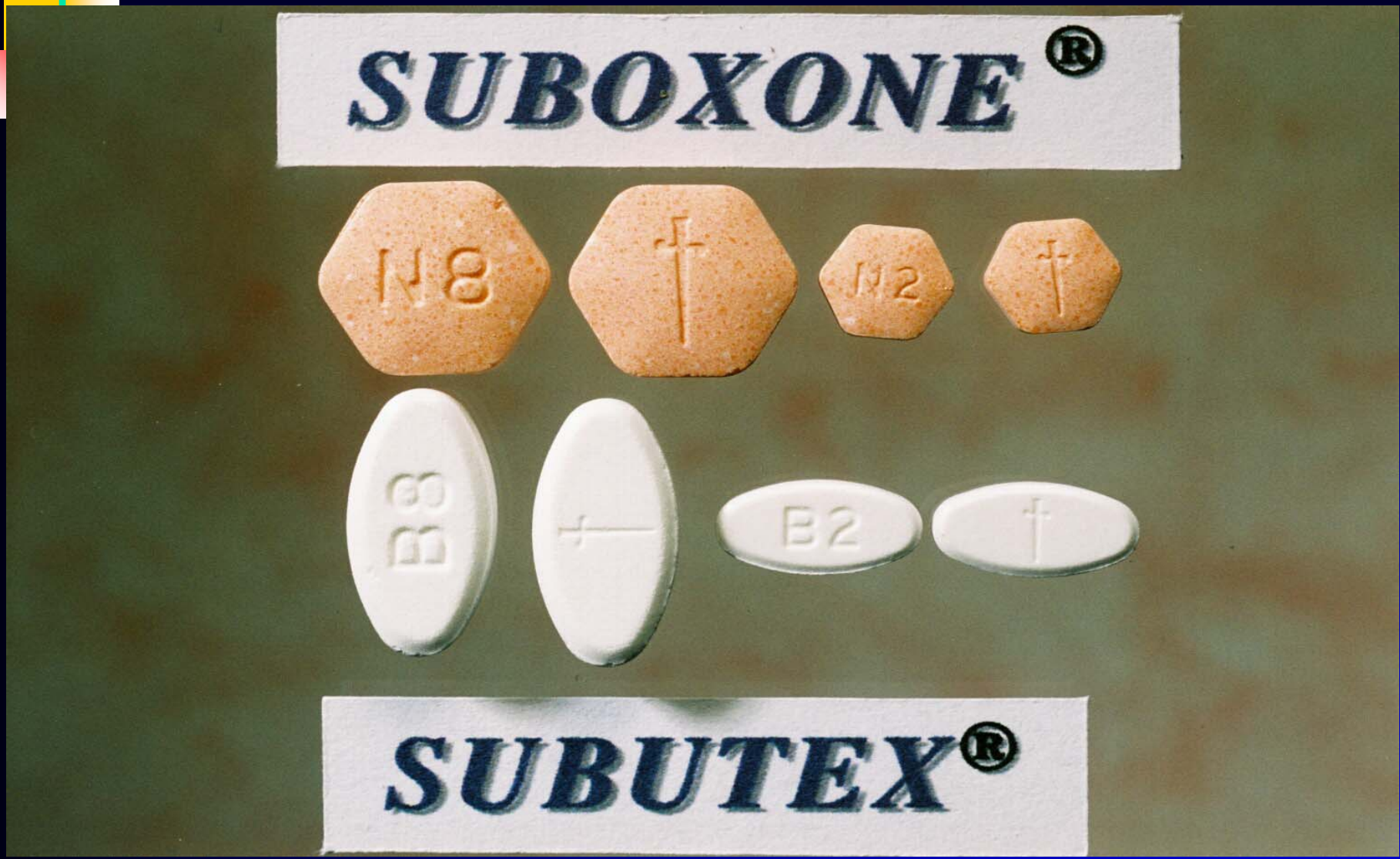
- Schedule III under the Controlled Substances Act
- Oval white tablet for sublingual administration
- Two dosage strengths
  - 2 mg buprenorphine
  - 8 mg buprenorphine

Drug Label for NDA 20-732 and NDA 20-733

Suboxone®

- Schedule III under the Controlled Substances Act
- Hexagonal orange tablet for sublingual administration
- Two dosage strengths
  - 2 mg buprenorphine with 0.5 mg naloxone
  - 8 mg buprenorphine with 2 mg naloxone

Drug Label for NDA 20-732 and NDA 20-733



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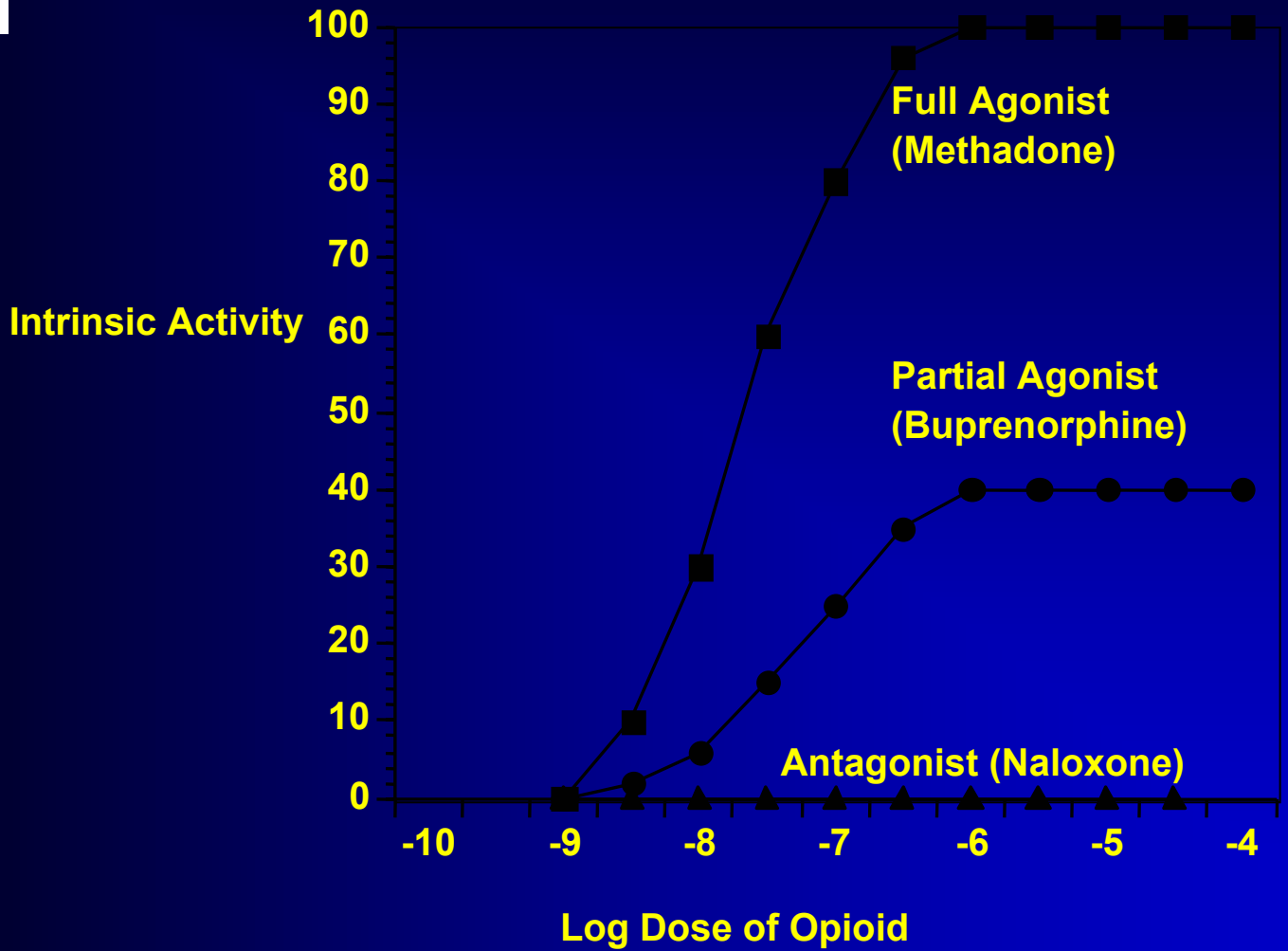
Buprenorphine: A Partial Agonist

Partial agonists:

- Bind to and activate receptor
- Increasing dose does not produce as great an effect as does increasing the dose of a full agonist (less of a maximal effect is possible)

Intrinsic Activity: Full Agonist (Methadone), Partial Agonist (Buprenorphine), Antagonist (Naloxone)



Affinity and Dissociation

Buprenorphine has:

- high affinity for mu opioid receptor –
  - competes with other opioids and blocks their effects
- slow dissociation from mu opioid receptor –
  - prolonged therapeutic effect for opioid dependence treatment

Bioavailability

- Good parenteral bioavailability
- Poor oral bioavailability
- Fair sublingual bioavailability
- For opioid dependence treatment:
  - early clinical trials used an alcohol-based solution
  - FDA approval for tablets that are held under tongue

Abuse Potential

- Buprenorphine is abusable (epidemiological, human laboratory studies show)
- Diversion and illicit use of analgesic form (by injection)
- Relatively low abuse potential compared to other opioids

Abuse Potential

Non-dependent opioid user

- Single doses of buprenorphine produce typical mu agonist effects
  - shown when given by injection and sublingual route
- Onset of effects slower for sublingual route (suggesting lower abuse potential)

Abuse Potential

Physically dependent opioid user

Abuse potential of buprenorphine varies as function of three factors:

1. Level of physical dependence
2. time interval between last dose of agonist and first dose of administered buprenorphine
3. dose of buprenorphine

Potential for Physical Dependence

- Repeated administration of buprenorphine produces or maintains physical dependence
- However, degree of physical dependence is less than that produced by full agonist opioids
- This means withdrawal syndrome should be less severe for buprenorphine

Sublingual Naloxone

- Sublingual naloxone has relatively poor bioavailability
- Dose up to 1-2 mg sublingual do not precipitate withdrawal in opioid dependent volunteers
- Sublingual naloxone does have a bitter taste

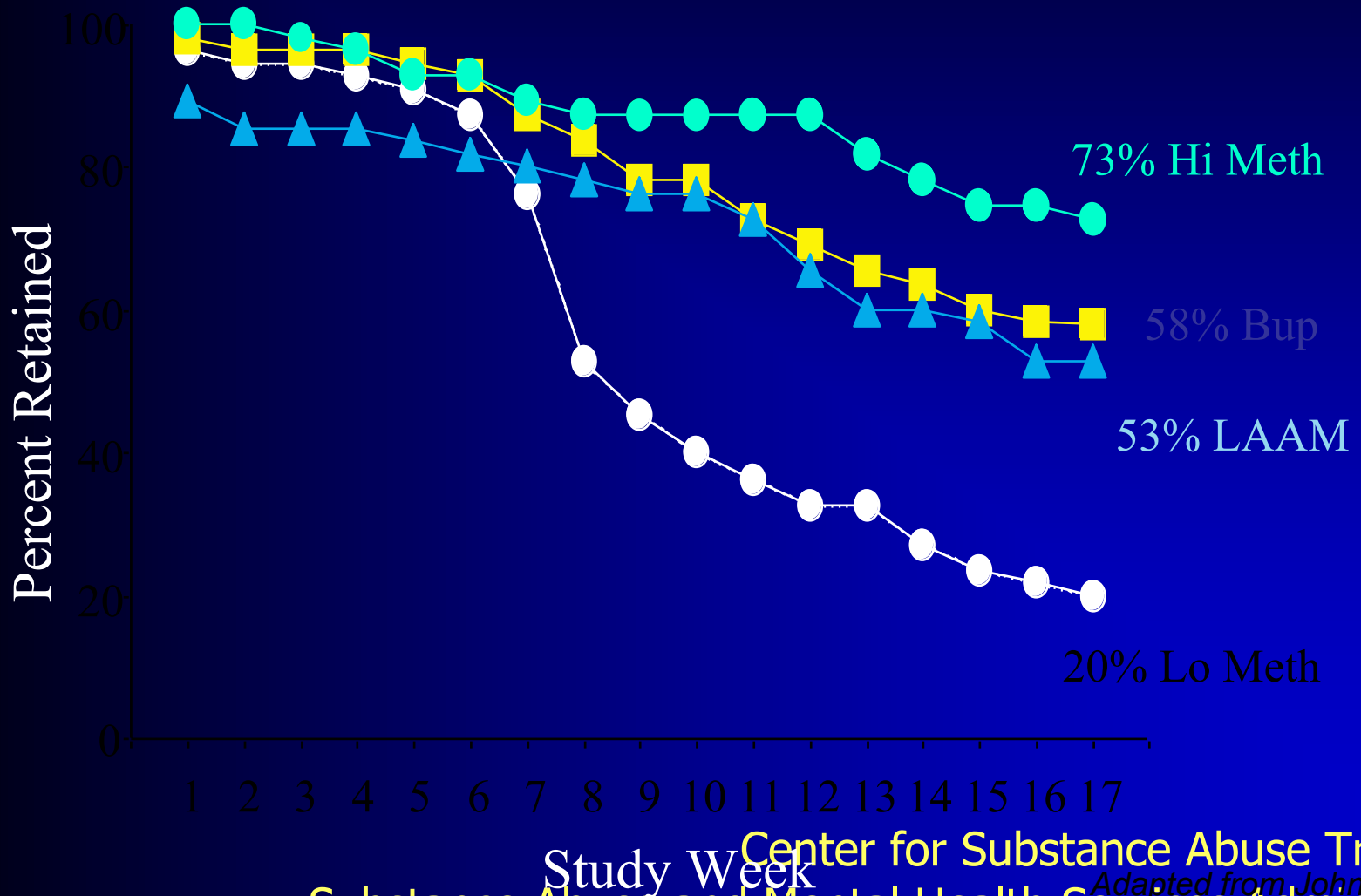
Combination of Buprenorphine plus Naloxone

- Sublingual buprenorphine has fair bioavailability
- Addition of naloxone to buprenorphine to decrease abuse potential of tablets
- Combination ratio is 4 to 1 (buprenorphine to naloxone)

Combination of Buprenorphine plus Naloxone

- Combination tablet containing buprenorphine with naloxone – if taken under tongue, predominant buprenorphine effect
- If opioid dependent person dissolves and injects buprenorphine/naloxone tablet – predominant naloxone effect (and precipitated withdrawal)

Buprenorphine, Methadone, LAAM: Treatment Retention



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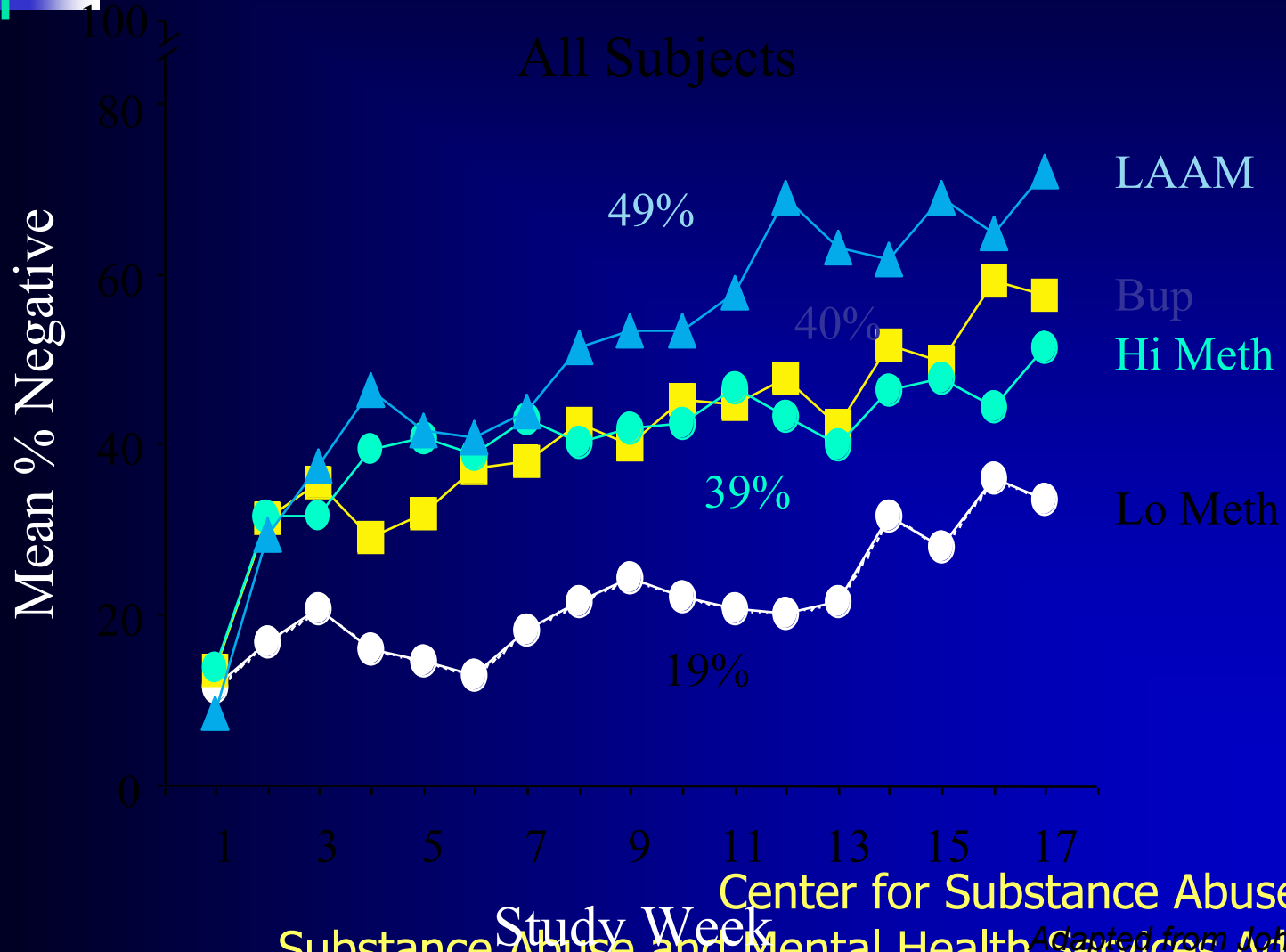
Adapted from Johnson, et al., 2000

Buprenorphine, Methadone, LAAM: Opioid Urine Results



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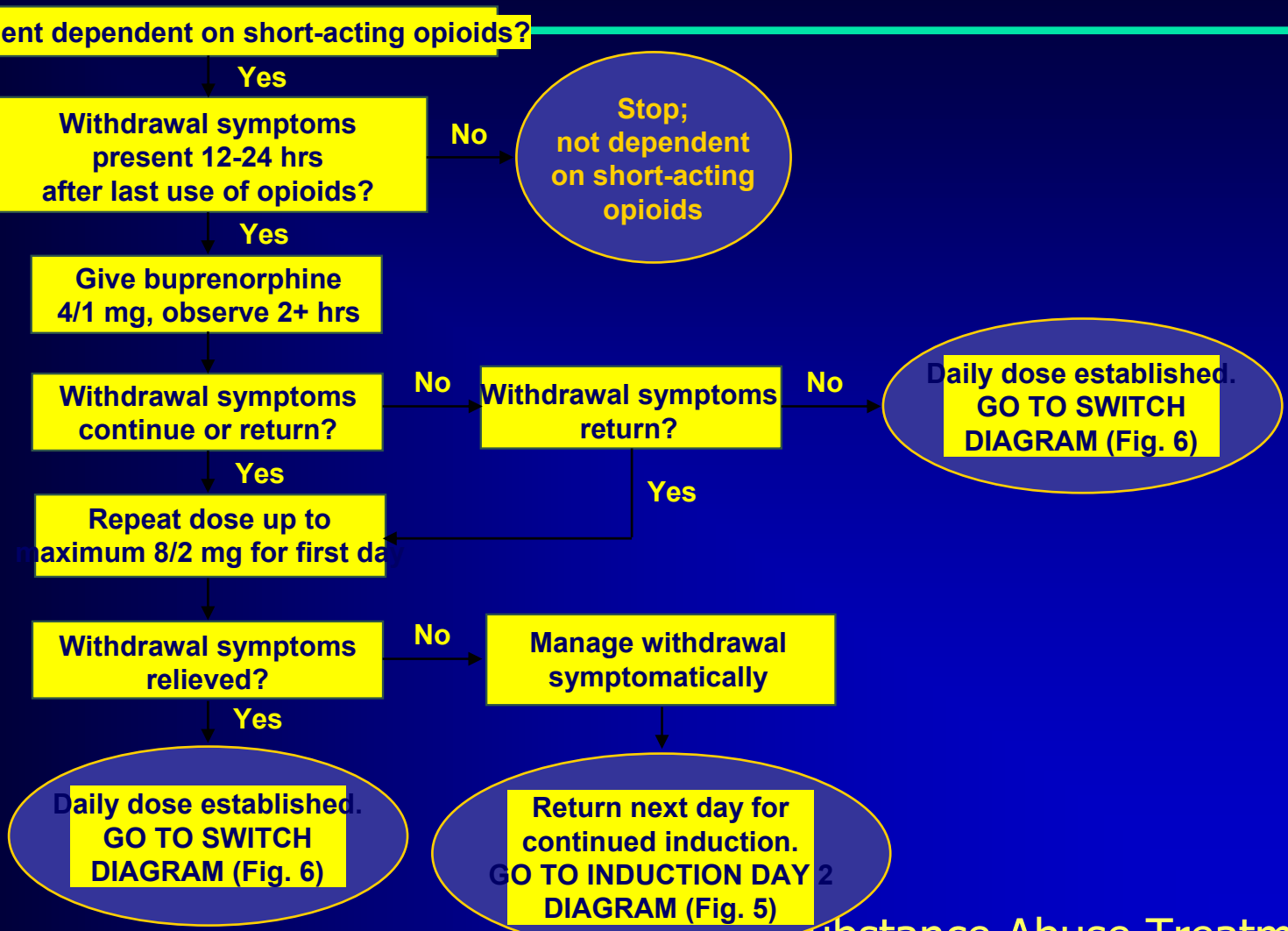
Adapted from Johnson et al., 2000

Buprenorphine Induction

Patients dependent on short-acting opioids

- Instruct patient to abstain from any opioid use for 12-24 hours (so they are in mild withdrawal at time of first buprenorphine dose)
- If patient is not in opioid withdrawal at time of arrival in office, then assess time of last use and consider either having him/her return another day or wait in the office until evidence of withdrawal seen

Figure 3: Induction for Patient Physically Dependent On Short-acting Opioids, Day 1



Buprenorphine Treatment Strategies

- Patients should be given the initial doses of BNP under supervision (~10-12mg/day)
  - Provider may choose to keep stock
    - May use routine supplier
    - May use Sponsor's supply (depending on state)
    - May Use Sponsor's help in
  - Keep medication in secure environment
    - Must have log book or record of disposition of all doses

Buprenorphine Warnings: Respiratory Depression

- Significant respiratory depression, particularly by the IV route of administration
- A number of deaths have occurred when addicts use IV, usually with benzodiazepines
- Deaths have occurred with co-use of alcohol, opioids or other depressants

Drug Label for NDA 20-732 and NDA 20-733

FDA Approval

- Info for Pharmacists
- Interactions (benzodiazepines)
- Multiple prescriptions
- Verification of Rx, Waiver
- Confidentiality

Pharmacists Verifying Waiver Status

- Online Physician Locator
  www.buprenorphine.samhsa.gov
- Lists made available to State regulatory and law enforcement agencies
- Phone directly to SAMHSA/CSAT
  - 301-443-0457
  - Info On Distribution
    866-282-2107

SAMHSA
Substance Abuse & Mental Health Services Administration
U.S. Department of Health and Human Services

Buprenorphine
PHYSICIAN LOCATOR

- home
- about the physician locator
- physician list search
- state substance abuse agencies
- frequently asked questions
- links
- comments or questions
- treatment facility locator

To locate the physician(s) authorized to prescribe Buprenorphine nearest you, find your **State** on the map below and click on it.

Questions from Pharmacists

- Use in in-patient detoxification
  - Permitted
- Buprenex?
- Detoxification/maintenance protocols
- Multi-registered physicians
- Nurse Practitioners/Physicians Assistants.

Oversight - Federal

- Waiver review/approval system
- DEA periodic inspections
- State Medical Boards – some revocations
  - FSMB Guidelines (www.fsmb.org)
    - Treatment plans
    - Documentation

Board Feedback on Draft Guidelines

2) Concerns about 42CFR2 (Federal Confidentiality Regulations):

- **Does this really apply to physicians? (YES)**
- **Does this prevent the Board from examining addiction treatment records or using them to prosecute physicians? (NO, but it does prevent you from using them to prosecute patients)**

42CFR2 (Fed Confidentiality) 1

- The term "program" means any person or organization that is federally assisted, and in whole or part, providing alcohol or drug abuse diagnosis, referral for treatment or treatment

42CFR2 (Fed Confidentiality) 2

- The term "Federal assistance" means receives Federal funds in any form, even when the funds do not pay for alcohol or drug treatment services
- Federally authorized to conduct business, such as licensed to provide methadone under NATA or w/Federal waiver for Schedule III-IV under DATA

Medical Board Still Has Authority

- Disclosure Exception under 42CFR 2 for Audit and Evaluation:
- Government agencies, peer review, insurance companies and others who regulate and fund treatment programs may have access to treatment records in order to conduct audit/evaluation
- Access granted without patient consent

Redisclosure is Limited, Patient is Still Protected Under 42CFR2

- May only <u>redisclose</u> pt identifying info:
  - 1. back to the program
  - 2. in response to a court order investigating the <u>program</u> (not the patient)
  - 3. To government agencies overseeing Medicare or Medicaid investigations
- All patient identifying information is to be destroyed after the audit and evaluation is completed

Redisclosure (cont.)

- Redisclosure without consent is limited exclusively to goal of the audit and evaluation
- To copy or remove records, investigators must certify that they will abide by 42CFR2

Uncertainties

- Drug availability – with distributors and in pharmacies
- Drug Cost – wholesale ~ $1/mg
- How will medication be distributed?
  - Demand driven
- How many physicians?
- How many patients?
  - Treated by physicians?
  - Treated in Opioid Treatment Program

Off-Label Use

- Not prohibited
- Not promoted for analgesia
- Addiction treatment dose greater
- Cost?
- Combination w/naloxone
- Pharmacists should verify all Rx w/out unique ID

Immediate use?

- Wait 45 days, or Rx/dispense immediately if:
- If facilitates treatment of an individual patient, and
- CSAT and DEA are notified.
- 25% of physicians indicate immediate use.

Post Approval Monitoring

- Post-Marketing surveillance - comprehensive risk management program designed to deter abuse and diversion from its legitimate use in patients and physicians regarding proper use of these drugs,
  - **Close monitoring** of drug distribution channels, and child resistant packaging.
  - **Active Surveillance -** Ethnographer Inverviews, media surveillance, treatment programs, reporting.

CSAT Determination

- Legislative
- Impact of waiver system on
  - Access to treatment
  - Public health consequences
- Includes Physician and other surveys
- Determine need for additional standards

Buprenorphine vs.Methadone

- Buprenorphine-Waivers
  - Prescribing
  - Federal law preempts state from precluding OBOT
  - Physician has capacity to refer for services
  - State Medical Board Licensing and Guidelines
- Methadone/LAAM/ Buprenorphine-OTPs
  - No prescribing
  - Federal law does not preempt state
  - Services must be provided directly or via formal documented agreement
  - Accreditation required

Summary/Conclusions

- Opiate Dependence/addiction Significant Public Health Problem
- Opioid Treatment – Significant changes
  - Federal regulations, accreditation
  - Buprenoprhine, new legislation
- Both modalities essential
- Training and education imperative so new modalities are introduced w/minimal risks.

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